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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/951,733	10/16/97	HARRINGTON L.	A-433B

EXAMINER	
BUGAISKY,G	
ART UNIT	PAPER NUMBER
1652	12

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US PATENT OPERATIONS NOA
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DATE MAILED: 01/07/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 10/20/98

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~or thirty days~~, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-32 is/are pending in the application.
Of the above, claim(s) 22-25, 31-32 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☐ Claim(s) _____ is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 6, 8
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-421-632/40206

DETAILED ACTION

Election/Restriction

Applicants's election with traverse of Group I in Paper No. 10 is acknowledged. The traversal is on the ground(s) that 80% of the claims in Group I are drawn to a composition of matter, and are not process of making claims. It is further stated that Applicants' invention is drawn to a new class of mammalian genes and the proteins encoded by these genes and that this discovery comprises a single unified invention. This is not found persuasive because first, unity of invention is used by WIPO and is currently not a concept of U.S. restriction practice unless an application has been filed under 35 U.S.C. § 371. Second, it is acknowledged that 80% of the claims in Group I are drawn to a composition: an isolated gene and constructs containing that gene; however, it is noted that the relationship between Groups I and II is that of process of making and Product made. The compositions recited in each group are patentably distinct inventions which have different functions. DNA and proteins are totally different molecules, are placed in different classes (DNA in class 536, whereas protein is placed in Class 530, or Class 435, if the protein has enzymatic activity.) and have non-overlapping mandatory searches. In the interest of compact prosecution, the Examiner did not place the process claims into a separate group, as the methods of making a recombinant protein by transformed cells is most easily searched with composition claims drawn to the DNA constructs.

The requirement is still deemed proper and is therefore made FINAL.

Claims 22-25 and 31-32 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 10.

Information Disclosure Statement

The Examiner has not considered references CC, ER, ES and EZ of Paper No:6, as these are books which have not been submitted; a table of contents is not sufficient for consideration of all the material within the book. While the oral disclosure of EO may be of great import, the Examiner cannot consider what has not been submitted.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acids encoding TP2 of SEQ ID NO: 14 and 20, and biologically active fragments thereof, and the disclosed mutations of the above gene. does not reasonably provide enablement for any other gene encoding a TP2 polypeptide or mutations at specific sites within other genes.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. First, the Examiner has noted the definition of "biologically active " which appears on page 15, lines 33-36 and page 16 lines 1-11, which specifies the active fragment must posses telomerase catalytic activity and have one of several recited properties. The instant fact pattern closely resembles that in Ex parte Maizel, 27 USPQ2d 1662 (BPAI 1992). In Ex parte Maizel, the claimed invention was directed to compounds which were defined in terms of function rather than sequence (i.e., "biologically functional equivalents"). The only disclosed compound in Ex parte Maizel was the full length,

naturally occurring protein. Similarly, the gene encoding the catalytic subunit of human telomerase is disclosed in the instant application. The Board found that there was no reasonable correlation between the scope of exclusive right desired by Appellant and the scope of enablement set forth in the patent application. Even though Appellant in Ex parte Maizel urged that the biologically functional equivalents would consist of proteins having amino acid substitutions wherein the substituted amino acids have similar hydrophobicity and charge characteristics such that the substitutions are "conservative" and do not modify the basic functional equivalents of the protein, the Board found that the specification did not support such a definition, and that the claims encompassed an unduly broad number of compounds. Such is the instant situation. Clearly, in this case, Applicants have disclosed a gene from a single species and defined specific mutations which alter the enzymatic activity of the encoded protein.

In *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). the issue of enablement in molecular biology was considered. There are eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. Although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable. Because there is but a single gene provided, minimal guidance to where one may vary the protein, no general teaching of the structures expected to be held in common with other TP2 gene, no suggestion where one may reasonably expect to find variant TP2s genes which still encode a functional telomerase, the examiner has concluded that one has been given an invitation to experiment to try to obtain another gene of different structure encoding a TP2.

With respect to the recited methods of claims 26-28, the disclosure is limited to altering telomerase activity by expression in host cells transformed with a human TP2 gene. The claims read upon altering endogenous telomerase activity , but the specification has no provided no methods to accomplish such in non-transformed cells. One has been given an invitation to experiment in order to alter proliferative rate or telomerase activity in non-transformed cells.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

Claims 1, 4, 7, 13, 19, and 26-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention.

TP-2 is vague as it is an abbreviation, is used by inventors for the purified gene encoding a polypeptide of the telomerase complex. A name of a protein in the absence of structural information (i.e., SEQ ID NO.) or functional characteristics does not serve to identify the claimed invention.

Claim 1 recites DNA molecules encoding proteins that have 90% sequence identity to specific SEQ ID Nos. Claims using language of the % sequence identity (similarity, homology, etc.) kind have been deemed indefinite when the disclosure does not include an explanation of how the calculation is made, the percentage algorithm to use and the parameters to set in the algorithm, e.g., gap penalties, mismatch penalties.

A table or figure exemplifying a sequence alignment and the numerical sequence identity, without more elaboration does not satisfy the need for explicit instructions on how to interpret the claims, because it is not possible to work backward from the example to derive the algorithm and parameters used. The examiner notes that the addition of information to the specification may be

considered new matter if adequate support is not present in the specification and claims as originally filed.

Further, the discussion of "high stringency conditions" on page 18, lines 5-18 and page 19 lines 1-12 is noted. The examples of stringent conditions are non-limiting examples. It is suggested that Applicants incorporate specific conditions into the claim.

Claims 7, 13 and 19 are included in this rejection as they depend from claim 1 and do not clarify the ambiguity.

Claim 4 is confusing , as in line 2, "SEQ ID NO:14 of SEQ ID NO:20" is recited. It is not clear if the "of" arose from a typographical error and should be "or" or whether some unknown phrase was omitted prior to the "of".

Claim 26 is confusing-what is meant by proliferation of a cell? Is not "proliferation rate" intended?

Claim 28 is confusing- what is meant by decreasing telomerase? Is it telomerase amount or enzymatic activity

With respect to claims 29 and 30, recitation of an amino acid position without reference to a SEQ ID NO: renders a claim indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 4, 6-8, 10, 12-14, 16 and 18-19 are rejected under 35 U.S.C. 102(a) as being anticipated by Nakamura *et al.* The reference describes the cloning of the putative catalytic subunit of both human and *Schizosaccharomyces pombe* telomerase. The gene is identical to the instantly described gene and encodes the same protein. Nakamura, however, place the start codon of the encoded protein at aa 23. Applicants are requested to confirm their start codon, as they have given HIS as the first codon. The Examiner has thus far not yet been able to review the 08/873039 priority document. Upon review, the reference may not constitute prior art. If the '039 document does not disclose the instantly claimed invention, then Applicants may be able to overcome this rejection with a declaration of possession prior to the publication date of the reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the

contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 5, 9, 11, 15 , 17, 21, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura *et al.* The reference is discussed above. They do not provide the specifically recited fragments nor the claimed methods. With respect to the claimed compounds and method of making a truncated protein, they define the shared sequence motifs with other reverse transcriptases; it would have been obvious for one of skill in the art to subclone regions of the gene. With respect to the claimed methods of altering proliferative activity, they show in Figure 3 that higher levels of telomerase mRNA are expressed in immortal vs. mortal cell lines. In order to change the proliferative capacity of a cell line, one of skill in the art would have found it obvious to place the gene of Nakamura et al. into cells, with a reasonable expectation of success in altering endogenous telomerase activity. As discussed above, the Examiner has thus far not yet been able to review the 08/873039 priority document. Upon review, the reference may not constitute prior art. If the '039 document does not disclose the instantly claimed invention, then Applicants may be able to overcome this rejection with a declaration of possession prior to the publication date of the reference.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Meyerson *et al.* was published shortly after Nakamura *et al*. and also report the cloning of the gee encoding the catalytic subunit of human telomerase.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Gabriele E. Bugaisky, Ph.D. whose telephone number is (703) 308-4201. The Examiner can normally be reached from 7:30 AM to 4:00 PM on weekdays.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Robert A. Wax, can be reached at (703) 308-4216.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center receptionist whose telephone number is (703) 308-0196.

CHARLES L. PATTERSON, JR.
PRIMARY EXAMINER
GROUP 1800

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December 24, 1998